REMARKS

Reconsideration of this application, as amended, is respectfully requested. New claims 51 and 52 have been added. With this amendment, claims 38-44, 46, 47, 51, and 52 are pending in this application. These amendments are made without prejudice or disclaimer, do not add new matter, and are supported by the originally filed specification. Consideration and entry of these amendments is respectfully requested. Applicants reserve the right to prosecute any amended, cancelled, or otherwise unclaimed subject matter in this or another application.

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 38-44, 46 and 47 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Schlom et al. (U.S. Pat. No. 6,045,802) in view of Matteucci (U.S. Pat. No. 4,923,808), Horig (Cancer Immunol. Immunother., 49: 504-514 (2000)), and Parmiani et al. (J. Natl. Cancer Inst., 94: 805-818 (2002)). Applicants respectfully disagree with these rejections, as set forth below.

The Office Action alleges that Schlom teaches the use of CEA (but not Applicants' SEQ ID NO.: 6) and B7 in a cancer vaccine and Matteucci teaches the use of silent mutations to change the nucleotide sequence that encode a protein without changing the amino acid sequence to provide improved protein production. The June 10, 2009 Office Action alleged that "[a]ll of the component parts are taught by Schlom et al. and Matteucci", the "only difference" between the claimed subject matter and what is taught by Schlom and Matteucci being "the combination of 'old elements' into a single expression system comprising SEQ ID NO. 6 and a nucleic acid sequence encoding human B7.1." The present Office Action concludes that, given these teachings, the skilled "artisan would have taken the wild type nucleic acid sequence of CEA, made silent mutations, and identified sequences that resulted in higher expression of CEA protein." As previously stated, Applicants believe this line of reasoning simply cannot support a proper *prima facie* case of obviousness.

Applicants have previously explained their belief that the line of reasoning set out in the Office Action is completely contrary to Pharmastem. Matteucci provides, at most, general guidance as to how to modify nucleic acid sequences, and a limited number of

specific examples of modified nucleic acid sequences. None of the cited references provide any guidance as to how or why the skilled artisan would have been motivated to modify the wild-type CEA nucleotide sequence to arrive at SEQ ID NO.:6. Matteucci provides no guidance whatsoever regarding which particular nucleotides should be modified to eliminate the problems related to expressing recombinant CEA. Applicants were the first to recognize a problem associated with expressing recombinant CEA, the solution to which is represented by SEQ ID NO.: 6. Neither Schlom nor Matteucci suggest modifying wild-type CEA (e.g., SEQ ID NO.: 1) in *any* way, much less in the *particular* way shown in SEQ ID NO.: 6.

As described at MPEP 2141, Office personnel are directed to "make a proper determination of obviousness under 35 U.S.C. 103, and to provide an appropriate supporting rationale in view of the recent decision by the Supreme Court in *KSR*". The "framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966)" requires consideration of at least: (1) the scope and content of the prior art; 2) the level of ordinary skill in the art; and, 3) the differences between the claimed invention and the prior art. Once these factual determinations are made, a conclusion regarding obviousness may be made based on any of several "exemplary rationales":

(A) Combining prior art elements according to known methods to yield predictable results;

(B) Simple substitution of one known element for another to obtain predictable results;

(C) Use of known technique to improve similar devices (methods, or products) in the same way;

(D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

(E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other

market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Applicants realize that the exemplary rationales listed above are noted at MPEP 2141 as not representing an "all-inclusive list". However, the Office Action has not provided any clear reasoning supporting the rejections as required by MPEP 2143 ("The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.") The Office Action merely provides conclusions. Applicants have therefore reviewed these exemplary rationales in an attempt to identify one supporting the conclusions of the Office Action.

Regarding example (A) (MPEP 2143), and as admitted in the Office Action, Applicants are not "combining prior art elements according to known methods to yield predictable results". Wild-type CEA, the nucleotides A, T, G and C, and Matteuci's method were known in the art. However, Applicants' SEQ ID NO.: 6, containing 246 nucleotide substitutions to the wild-type CEA sequence, was not. Thus, it cannot be shown "that the prior art included each element claimed".

And Applicants have not engaged in the "[s]imple substitution of one known element for another to obtain predictable results" because the elements of the claimed subject matter simply did not exist (MPEP 2143, example (B)). As described above, wild-type CEA, the nucleotides A, T, G and C, and Matteuci's method were known in the art. However, Applicants' SEQ ID NO.: 6 containing 246 nucleotide substitutions was not. As such, the elements to be substituted were not both known, making the "simple substitution" of one for the other impossible. Thus, it cannot be shown "that the substituted components and their functions were known in the art".

The Office Action has not shown that Applicants' claimed subject matter is simply a "base" product that has been improved in the same manner as a "comparable" product (MPEP 2143(C)). The Office Action does not describe any "comparable" product. Matteuci does not relate to modification of wild-type CEA. Schlom does not provide any suggestion to "improve" wild-type CEA. In fact, Schlom describes that

using wild-type CEA "led to an enhanced T-cell immune response specific for CEA" (col. 19, lines 8-13), leaving the skilled artisan no motivation to improve that sequence. Applicants believe they were the first to even recognize a problem associated with expression of wild-type CEA in poxviral vectors. As such, the skilled artisan would not have had any motivation to look to methods such as that of Matteucci to improve the nucleotide sequence encoding wild-type CEA.

Example D ("[a]pplying a known technique to a known device (method, or product) ready for improvement to yield predictable results") is similarly inapplicable. It cannot be shown "that one of ordinary skill in the art would have recognized that applying the known technique would have yielded predictable results and resulted in an improved system." MPEP 2143(D). The skilled artisan had no reason to apply Matteuci's methods to wild-type CEA to produce SEQ ID NO.: 6. The Office Action has not shown that the skilled artisan had any reason to modify wild-type CEA. As described above, Schlom was successful using wild-type CEA leaving the skilled artisan no reason to look further. Therefore, application of Matteuci's method to wild-type CEA would not have been recognized as useful in the field. As such, rationale (D) is not applicable.

The Office Action similarly has not shown that the modified CEA sequence shown in SEQ ID NO.: 6 would have been "obvious to try" (MPEP 2143(E)). It has not been shown that SEQ ID NO.: 6 resulted from a choice from among a finite number of identified, predictable solutions, with a reasonable expectation of success. As discussed above, the Office Action has not shown that the problem Applicants solved was even recognized by the prior art. As such, there would have been no motivation "to try" modifying wild-type CEA. And, while wild-type CEA, the nucleotides A, T, G and C, and Matteuci's method were known in the art, the 246 nucleotide modified in SEQ ID NO.: 6 simply cannot be said to have been either "identified" nor "predictable" as of Applicants' filing date.

The Office Action has also failed to show that "[k]nown work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art" (MPEP 2143(F)). In fact, the cited references are related to similar fields of study. And the Office Action does not point to anything in the cited

references that would "prompt variations" to, for example, wild-type CEA to provide SEQ ID NO.: 6. As previously mentioned, Schlom describes how the use of the compositions described therein "led to an enhanced T-cell immune response specific for CEA" (col. 19, lines 8-13). Given Schlom's success, the skilled artisan would not have been motivated by "design incentives or other market forces" to modify those compositions. The compositions containing wild-type CEA were shown by Schlom to produce the desired effect, leaving the skilled artisan with no motivation to modify the same.

Finally, the Office Action has not provided any description of a "teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention." The Office Action merely concludes that "artisan would have taken the wild type nucleic acid sequence of CEA, made silent mutations, and identified sequences that resulted in higher expression of CEA protein." The Office Action does not provide any reasons why the artisan would have done so. As discussed above, Schlom successfully used wild-type CEA to produce an immune response and provided no suggestion to modify that sequence. Simply concluding that the skilled artisan would have modified wild-type CEA without a description of some motivation to do so is not consistent with the requirements described at MPEP 2143 (e.g., "[t]he key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.".

The rejection does not present a legally sufficient *prima facie* showing of obviousness regarding SEQ ID NO.: 6, which is clearly a key feature of the claimed subject matter. And neither Horig nor Parmiani cure the deficiencies in the combination of Schlom and Matteucci. As such, Applicants respectfully request withdrawal of these rejections.

CONCLUSIONS

Reconsideration of this application, as amended, is respectfully requested. A Notice of Allowance for all claims is also respectfully requested. The Examiner is encouraged to contact the undersigned if it is believed doing so would expedite prosecution.

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